FACTORS INFLUENCING PHYSICIAN'S DECISION ON GENERIC STATIN PRESCRIPTION: DISCRETE CHOICE EXPERIMENT

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FACTORS INFLUENCING PHYSICIAN'S DECISION ON GENERIC STATIN PRESCRIPTION: DISCRETE CHOICE EXPERIMENT

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ABSTRACT

Statin drugs are the most frequently prescribed drugs for dyslipidemia in Thailand. Substantial savings could be achieved by statin generic substitution. Regarding this, physicians are key people who can decide whether patients receive either a brand-name or generic drug. **U**nderstanding the preferences of physicians is essential for promoting generic drug prescription in the hospital. This study aims to use a Discrete Choice Experiment (DCE) to examine 1)preference for generic statin drug prescription, 2) attitude towards generic drugs, and 3) the knowledge regarding the price of statin of family physicians at Ramathibodi Hospital. A cross-sectional survey using DCE was conducted. A self-administrated questionnaire was distributed to all family medicine physicians at the Department of Family Medicine, Ramathibodi Hospital from July toAugust, 2014. According totheliterature review and expert opinions,the followingfour attributes were selected for DCE: prevention from Coronary Heart Disease (CHD) and Framingham Risk Score, cost difference between statin original drug and generic drug per day, LDL cholesterol level and health insurance scheme. Nine choice sets were developed. Each choice set comprised two scenarios. For each choice set, physicians were asked "For which scenario would you prescribe a generic statin drug?"There was an overall response rate of 56.52% (26/46). In general, most family physicians in the study havea positive attitude towards generic drugs. Regarding knowledge of statin price, about 57.7% of physicians do not know the price of the statins. Regarding preferences for generic statin prescribing, the cost difference between the generic and brand name drug as well as the insurance scheme of the patients are associated with physicians' decision to prescribe generic statin. It was found that physicians preferred to prescribe generic statin if there was a very high cost difference between the generic and original drug, as compared to low or high cost difference. In addition, physicians preferred to prescribe generic statin to self-pay patients more than CSMBS patients. To promote the use of generic substitution, a policy to support generic substitution should be developed and knowledge on drug prices should be provided.

KEY WORDS: GENERIC DRUG/DISCRETE CHOICE EXPERIMENT/ PHYSICIAN/ ATTITUDE/ STATIN

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ปัจจัยที่มีผลต่อการตัดสินใจของแพทย์ในการสั่งจ่ายยาสตาตินสามัญ:ดีสครีต ช้อยส์เอ็กซ์เปอร์ริเมนท์

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บทคัดย่อ

ยากลุ่มสแตตินเป็นกลุ่มยาที่มีการสั่งจ่ายในคนไข้ภาวะไขมันในเลือดสูงมากที่สุดในประเทศไทย การจ่ายยาสามัญทดแทนในกลุ่ม สแตตินนั้นสามารถช่วยลดค่าใช้จ่ายดังกล่าวได้ โดยในกรณีนี้แพทย์คือบุคคลสำคัญที่จะตัดสินใจว่าผู้ป่วยสมควรได้รับยาต้นแบบหรือยาสามัญ ความเข้าใจถึงความพึงใจของแพทย์มีความสำคัญในการส่งเสริมการสั่งจ่ายยาสามัญในโรงพยาบาล การศึกษานี้ใช้ Discrete choice experiment (DCE) เพื่อศึกษาถึงความพึงพอใจของแพทย์ในการสั่งจ่ายยาสามัญกลุ่ม สแตติน, วิเคราะห์หาทัศนคติของแพทย์ต่อยาสามัญ และวิเคราะห์ถึงความรู้ของแพทย์เกี่ยวกับราคายากลุ่ม สแตตินของแพทย์ภาควิชาเวชศาสตร์ครอบครัว โรงพยาบาลรามาธิบดี การสำรวจเป็นแบบภาคตัดขวางโดยใช้ DCE ซึ่งแบบสอบถามได้ถูกแจกจ่ายให้กับแพทย์ทุกคนในภาควิชาเวชศาสตร์ครอบครัว โรงพยาบาลรามาธิบดีในระหว่างเอนกรกฎาคม 2557 ถึง สิงหาคม 2557 จากการทบทวนวรรณกรรมและสอบถามความคิดเห็นจากผู้เชี่ยวชาญ คุณลักษณะ 4 คุณลักษณะ ต่อไปนี้ได้ถูกคัดเลือกมาเพื่อสร้าง แบบสอบถาม DCE: การป้องกันโรคหลอดเลือดหัวใจและframingham risk score, ราคาที่แตกต่างกันระหว่างยา สแตติน ต้นแบบและยาสามัญ, ระดับไขมัน LDL และสิทธิประกันสุขภาพ 9 ชุดคำถามถูกพัฒนาขึ้น โดยในแต่ละชุดคำถามจะประกอบด้วย 2 สถานการณ์ ในแต่ละคู่ของสถานการณ์แพทย์จะถูกถามว่า "จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug) สแตตินในสถานการณ์ใด" อัตราการตอบกลับทั้งหมดคิดเป็น 56.52% (26/46) โดยทั่วไปพบว่าแพทย์ส่วนใหญ่ในภาควิชาเวชศาสตร์ครอบครัวมีทัศนคติที่ดีต่อการใช้ยาสามัญ อย่างไรก็ตามพบว่าร้อยละ 57.7 ของแพทย์ไม่ทราบราคาของยากลุ่ม สแตตินในด้านเรื่องของความพึงใจในการสั่งจ่ายยาสามัญกลุ่ม สแตตินราคายาที่แตกต่างกันของยาต้นแบบและยาสามัญและสิทธิประกันสุขภาพของผู้ป่วยนั้น เกี่ยวข้องกับการตัดสินใจที่จะจ่ายยาสามัญกลุ่ม สแตตินโดยพบว่าแพทย์พึงใจที่จะสั่งจ่ายยาสามัญกลุ่ม สแตตินในกรณีที่ราคายาของยาต้นแบบและยาสามัญแตกต่างกันสูงมาก เมื่อเทียบกับราคาที่แตกต่างกันน้อยหรือสูง นอกจากนั้นยังพบว่าแพทย์พึงใจจะสั่งจ่ายยาสามัญกลุ่ม สแตตินในกรณีที่ผู้ป่วยชำระเงินค่ารักษาพยาบาลหรือค่ายาเองมากกว่าผู้ป่วยกลุ่มข้าราชการ นโยบายในการสนับสนุนการจ่ายยาสามัญทดแทนในข้าราชการควรได้รับการส่งเสริม นอกจากนั้นยังควรส่งเสริมการให้ความรู้แพทย์ทางด้านราคายาอีกด้วย

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LIST OF ABBREVIATIONS

GDP	=	Gross Domestic Product
WHO	=	The World Health Organization
ACA	=	American College of Cardiology
AHA	=	American Heart Association
CSMBS	=	Civil Servant Medical Benefit Scheme
SSS	=	The Social Security Scheme
UCS	=	The Universal Coverage Scheme
DCE	=	Discrete Choice Experiment

CHAPTER I
INTRODUCTION

The rapid growth on health care expenditure is a major problem in many countries including Thailand. Data from Ministry of Public Health indicated that Thai's health care expenditure increased from 25,315 million baths (3.8 % of gross domestic product-GDP) in 1980 to 588,154 million baths (6.4 % of GDP in 2008). (1) It was also found that drug expenditure represented a significant proportion of the total health expenditures in Thailand (approximately 46.4 per cent in 2008). (1) The increasing awareness of drug expenditure has reach to the rising use of policy-driven substitution original drugs to local made drugs. (2-3)

A generic drug is a medicine that is composed of the identical medicinal ingredients like brand-name drug, however it may be composed of unidentical non-medicinal ingredients. Using of generic medicine was broadly encouraged by the World Health Organization (WHO) according to their relatively lowering price compared with innovator products. (3)In addition, generic drug utilization is a mechanism for reducing drug expenditure in many countries for example the United Kingdom, the United States, the Netherlands, Germany, Denmark and Canada. (3-4)

Dyslipidemia is one of an independent risk factor for cardiovascular disease, which was the third cause of mortality among Thai population during 2008-2012, after malignant neoplasm and accident, respectively. (5) For treatment of dyslipidemia, statin drug, which reduces level of cholesterol by competitively inhibiting HMG-CoA reductase activity in liver, accounted for a major part of lipid-lowering drug expenditures in the global market. (2) Statin global market were expanded from US$ 34.2 billion in 2008 to US$ 37.7 billion in 2010 and slightly decrease to US$ 33.6 billion in 2012. (6) In 2012, Crestor ® (rosuvastatin) and Lipitor® (atorvastatin) were ranked the 3rd and the 14th of the top 20 global products, respectively. (7)

In Thailand, statin drugs are the highest frequently prescribed medicines for dyslipidemia. The Lipid Treatment assessment Project II (LTAP-II) study showed that 64% of Hyperlipidemia patients from 48 hospitals across Thailand were prescribed with statins. (8) Study from Ramathibodi hospital presented that statin expenditure was increasing 35.6% in 2006 and another 6.4% in 2007. Ramathibodi hospital database also indicated that statin drugs alone were accounted for 6.23, 7.12, and 6.15% of the total drug expenditure in 2005, 2006, and 2007 respectively. (9) It was also found that statins' expenditure increased largely from outpatients of civil servant that were more likely to be prescribed with original drugs. (9) Since September 2009, Ramathibodi hospital has introduced mandatory generic substation (228 items) for inpatient department. After the policy was implemented, more brand-name drugs including statins were switched to generic with potential cost saving about 10.1 million US$ per year. (10) However, substitution was not applied to Civil servants and self-pay patients receiving care at outpatients department.

Although some patients and physicians have expressed their concern about the effectiveness of generic medicines, this may be not an important issue as generic medication need to undergo a rigorous FDA approval process and must prove that they are bioequivalent to their brand-name counter parts. (11-15) Several studies comparing branded statin with their generic have found them to be clinically equivalent. (16-20) In Thailand, previous studies also confirmed the bioequivalence of generic statin to its brand-name product. (18, 21) Furthermore, evidences clearly indicated that the use of generic medicine is composed of the identical active ingredient as original drugs significantly reduce the drug expenditure, especially in case of statin. (10, 22-24) Previous study also indicated that adherence to statin therapy improved after switching to generic statin. (25) As the result, statin generic drug utilization should be promoted to increase efficient use of the limited health care resources. (9-10, 26)

Physician is certainly an essential key in determine whether patients receive either generic or original drug. (27) Physician can prevent unwarranted and excessive health care system spending by using generic drug. (10, 26) Previous study indicated that opinion on generic's efficacy and effectiveness (28), patient's income (28) and insurance coverage (28) as well as the medicine price (28) , are important factors influencing physician's decision to prescribe generic drugs. (28)

Understanding factors affecting physician decision to prescribe generic statin is essential to develop an effective strategy to promote generic drug utilization practice. However, very little is known about this issue in Thailand. In our study, statin is chosen as it is a commonly prescribed drug class for lipidemia. Also, statin is accounted for a major part of lipid-lowering drug expenditures in several hospitals including Ramathibodi hospital. In addition, it requires long-term utilization and has multiple generic options available.

Objectives

The objectives of this study are

1. to examine factors affecting family physicians' decision to prescribe generic statin drug,
2. to assess the attitude towards generic drugs among family physicians, and
3. to assess the knowledge of family physicians about price of generic and branded statin drugs.

Expected outcomes and benefits

The findings from this study can be use as an important input to generate effective policy to promote generic substitution especially in case of statin drugs.

Definition of terms

Original drug

An original drug is a medicine marketed under a proprietary, trademark-protected name

Generic drug

Generic drug is a medicine that is composed of the same medicinal ingredients as the original medicine, but may contain different non-medicinal ingredients.

Discrete choice experiment

Discrete choice experiment is an attribute-based survey method for measuring benefits (utility). Discrete choice experiments present respondents with hypothetical scenarios (choice sets) drawn from all possible scenarios (choice sets) accordance with statistical design principles. The choice sets were composed of two or more alternatives, which depend on attributes or characteristics of interest, and respondents have to choose one alternative.

CHAPTER II
LITERATURE REVIEW

This chapter consisted of 5 parts as follows;

2. 1 Dyslipidemia

2. 2 Health system in Thailand

2.3 Generic policy

2.4 Factors influencing generic prescribing of physicians

2.5 Discrete choice experiment

2.1 Dyslipidemia

2.1.1 Dyslipidemia

Cardiovascular disease (CVD) is the major cause of disability-adjusted life years (DALYs) and mortality in Europe, and also in many developing countries. (29)There are several risk factors of CVD. Many of these factors are associated with behavior, for example dietary habits, lack of exercise. In fact, CVD risk factors can be classified into modifiable, for example dyslipidemia, high blood pressure and type2 diabetes mellitus, or non-modifiable, such as male gender and age.

Dyslipidemia, characterised as the lipid abnormalities, is one of the risk factor for cardiovascular disease. Treatment and prevention of dyslipidemia should be considered for both primary and secondary prevention of cardiovascular disease.(30)

Increase of low-density lipoprotein-cholesterol (LDL-C) and total cholesterol (TC) can be changed by both medicine treatment and lifestyle modification. The evidence from multiple randomized controlled trials (RCTs)showed that decreasing of LDL-C and TC can prevent CVD. As the result, LDL-C levels and TC are first targets of CVD prevention and treatment.(30)

2.1.2 Risk assessment and classification of Cholesterol

The objective of the prevention is to lower the risk. Therapy adjustment will depends on absolute risk of patients. In general, LDL-C is used to define risk status of patient.

The association between coronary heart disease and LDL cholesterol levels is continuous over a wide range of LDL cholesterol levels. Hence, Adult Treatment Panel III (ATP III) improves the classification of total cholesterol levels, LDL cholesterol levels and HDL cholesterol levels, as shown in Table 2.1.

Table 2.1 ATP III Classification of LDL, Total, and HDL Cholesterol (31)

LDL Cholesterol(mg/dL)	**Risk**
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol (mg/dL)	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol (mg/dL)	
<40	Low
≥60	High

Determinants of risk in addition to LDL-cholesterol include the followings:

1. Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals (31)
2. Cigarette smoking
3. Hypertension (BP 140/90 mmHg or on antihypertensive medication)
3. Low HDL cholesterol (<40 mg/dL)
4. Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
5. Age (men 45 years; women 55 years)

Based on these other risk determinants, Adult Treatment Panel III ATP III presents three classes of risk which improve the modalities and goals of LDL-reduction treatment. Table 2.2 shows categories and presents corresponding LDL-cholesterol goals.

Table 2.2 Three Categories of Risk that Modify LDL Cholesterol Goals (31)

Risk Category LDL Goal (mg/dL)	
CHD and CHD risk equivalents	<100
Multiple (2+) risk factors	<130
Zero to one risk factor	<160

From the NCEP guideline, the category of highest risk composes of CHD and CHD risk equivalents. The latter show a risk for main coronary events equal to that of established CHD, i.e., >20% per 10 years (i.e., more than 20 of 100 such individuals will develop CHD or have a recurrent CHD event within 10 years). CHD risk equivalents comprise: (31)

1. Other clinical forms of atherosclerotic disease (symptomatic carotid artery disease, peripheral arterial disease and abdominal aortic aneurysm)
2. Diabetes mellitus
3. Multiple risk factors that confer a 10-year risk for CHD >20%.

Patients with CHD risk or CHD equivalents have the lowest LDL cholesterol goal (<100 mg/dL). The second category composes of patients with multiple (2+) risk factors in person, who has 10-year risk for CHD, is 20%. Framingham risk scores determine a risk. The presence of multiple risk factors that improve the goals of treatment and cutpoints for LDL-lowering therapy is determined bythe major risk factors, exclusive of increased LDL cholesterol, and these are shown in Table 2. <130 mg/dLis the LDL cholesterol goal for patients with multiple (2+) risk factors. The third category consists of patients having 0-1 risk factor; with little exceptions, persons in this classification have a 10-year risk <10%. <160 mg/dL is their LDL cholesterol goal (31).

2.1.3 Primary and secondary Prevention with LDL-Lowering Therapy

1. Primary prevention**;** Aim of primary prevention is to prevention the onset of specific diseases via risk reduction. Targets of primary prevention are adult patients without a diagnosis of cardiovascular disease (CVD) or CHD. Primary prevention of CHD presents the highest important opportunity for decreasing the burden of CHD. The public health approach reveals that the clinical approach to primary prevention which calls for behavior changes, including: 1) decreased intakes of saturated cholesterol and fat, 2) raised physical activity, and 3) weight control, to reduce cholesterol levels of population and decrease CHD risk, but the clinical approach intensifies preventive strategies for higher risk persons. One objective of primary prevention is to decrease long-term risk (>10 years) as well as short-term risk (10 years). LDL goals of treatment in primary prevention depend on a person's absolute risk for CHD. Recent primary prevention trials show that coronary death even in the short term and major coronary events risk is decreased by LDL-lowering drugs.

2. Secondary prevention; Early finding and treating disease is target of secondary prevention. Goals of secondary prevention are patients who established cardiovascular disease (angina pectoris, coronary heart disease, myocardial infarction, transient ischaemic attacks, cerebrovascular disease (CeVD) or peripheral vascular disease (PVD) or after coronary revascularization or carotid endarterectomy) are at very high risk of developing recurrent cardiovascular events. Secondary prevention target of LDL cholesterol is <100 mg/dL, is identified by Adult Treatment Panel III (ATP III). (31)

2.1.4 Drug treatment

Several groups of drug are used in treatment of dyslipidemia. These include statin (inhibiting HMG-CoA (or 3-hydroxy-3-methylglutaryl-coenzyme A) reductase activity), Bile acid Sequestrants, Nicotinic acid and Fibric acids (shown in Table 2.3.). However, the goal LDL-C level can be obtained from medicine monotherapy in many patients, a proportion of high risk persons with very high LDL-C levels or decreasing side effect from drugrequire additional treatment. Some of

patients who are not able to tolerate higher statin doses or are statin intolerant, physicians should be considered combination therapy.

Table 2.3 Drugs Affecting Lipoprotein Metabolism (31)

Drug class, agent and daily doses	**Lipid/Lipoprotein effects**	**Side effects**	**Contraindications**	**Clinical trial results**
HMG CoA reductase inhibitors (statins)*	LDL ↓18-55% HDL ↑5-15% TG ↓7-30%	Myopathy Increased liver enzymes	Absolute: • Active or chronic liver disease Relative: • Concomitant use of certain drugs†	Reduced major coronary events, CHD deaths, need for coronary procedures, stroke, and total mortality
Bile acid Sequestrants‡	LDL ↓15-30% HDL ↑3-5% TG No change or Increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta-lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL	Reduced major coronary events and CHD deaths
Nicotinic acid¥	LDL ↓ 5-25% HDL ↑15-35% TG ↓20-50%	Flushing Hyperglycemia Hyperuric	Absolute: • Chronic liver disease • Severe gout	Reduced major coronary events,

Table 2.3 Drugs Affecting Lipoprotein Metabolism (31) (cont.)

		emia (or gout) Upper GI distress Hepatotoxicity	Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease	and possibly total mortality
Fibric acids§	LDL ↓5-20% (may be increased in patients with high TG) HDL ↑10-20% TG ↓20-50%	Dyspepsia Gallstones Myopathy Unexplained non-CHD deaths in WHO study	Absolute: • Severe renal disease • Severe hepatic disease	Reduced major coronary events

* Lovastatin (20-80 mg), pravastatin (20-40 mg), simvastatin (20-80 mg), fluvastatin (20-80 mg), atorvastatin (10-80 mg), cerivastatin (0.4-0.8 mg).
† Cyclosporine, macrolide antibiotics, various antifungal agents and cytochrome P-450 inhibitors (fibrates and niacin should be used with appropriate caution).
‡ Cholestyramine (4-16 g), colestipol (5-20 g), colesevelam (2.6-3.8 g).
¥ Immediate release (crystalline) nicotinic acid (1.5-3 g), extended release nicotinic acid (Niaspan ®) (1-2 g), sustained release nicotinic acid (1-2 g).
§ Gemfibrozil (600 mg BID), fenofibrate (200 mg), clofibrate (1000 mg BID).

ACC/AHA Guideline 2013 determines the strength of statin treatment on the expected LDL–Cholesterol response to a specific statin and strength. Intensity of statin were determined to "High-intensity," "moderate-intensity," and "lower-intensity". Intensity of statin therapy was modified by the systematic reviews. Intensity of statin was classified by the percent of LDL–C level reduction. In addition, there is no difference in the types of statin and doses used for primary and secondary prevention. Intensity of statin was shown in Table 2.4.

Table 2.4 High- Moderate- and Low-Intensity Statin Therapy (32)

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin 40–80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20–40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg

2.1.5 Statin

Statin accounted for a major part of lipid-lowering drug expenditures in many countries including Thailand. (22) Nine statins have received approval from the US Food and Drug administration since 1987 (Lovastatin, simvastatin, pravastatin, fluvastin, mevastatin, rosuvastatin, pitavastatin, atorvastatin, and cerivastatin – withdrawn in 2001). (26) Among 8 statins available in the market, 5 are sold as generics, 2 are only available as brands (rosuvastatin, and pitavastatin).

During the past decade, a substantial health care expenditure was spent for brand-name statins. Brand revenues reduced by 20% in 2007 when the first generic simvastatin got into the market after Zocor® (simvastatin, Merck& Co Inc) losts its patients. (33) However, continued spending on Lipitor® (atorvastatin calcium; Pfizer

Inc) despite cheaper generic availability made it become the best-selling medication in history. (34-35) While generic atorvastatin has reduced the cost gap, it still priced above other generic statin.

In Thailand, the release of a generic version of simvastatin and atorvastatin amorphous form in 2006and 2011 showed animportant opportunity to improve accessibility of statin as well as to reduce unnecessary cost. In Ramathibodi hospital, six statins are available (simvastatin, atorvastatin, rosuvastatin, fluvastatin, pitavastatin and pravastatin). In Thailand, simvastatin and atorvastatin are available in both original and generic form. On the other hand, pravastatin (Mevalotin®), rosuvastatin (Crestor®), fluvastatin (Lescol®), and pitavastatin (Livalo®) are available in original form only. (36) Table 2.5 shows statin price in Ramathibodi hospital. It was found that Simvastatin price range from 1 Baht to 40 Bath while atorvastatin price range from 25.5 Baht to 58.5 Baht.

Table 2.5 Statin price in Ramathibodi hospital (36)

Simvastatin		Atorvastatin	
Trade name	Price (bath)	Trade name	Price (bath)
Zocor ® 20 Mg	40	Lipitor ® 10 Mg	40
Zocor ® 40 Mg	40	Lipitor ® 20 Mg	52.5
Bestatin ® 10 Mg	0.5	Lipitor ® 40 Mg	58.5
Bestatin ® 20 Mg	1.5	Xarator ® 10 Mg	25.5
Bestatin ® 40 Mg	1	Xarator ® 20 Mg	29.5
		Xarator ® 40 Mg	38.5

In Thailand, statin drugs are the highest frequently prescribed drug in dyslipidemia. From the Lipid Treatment assessment Project II (LTAP-II) study showed that statins were prescribed in 64% of Hyperlipidemia patients from 48 hospitals. (8) Study from Ramathibodi hospital in Thailand, presented that statin expenditure was rising 35.6% in 2006 and another 6.4% in 2007. Ramathibodi hospital database indicated that statin drugs group alone accounted for 6.23, 7.12, and 6.15% of the total drug expenditure in 2005, 2006, and 2007 respectively. (9) It was also found that statins' expenditure increasing generally from outpatients of civil servant that are

more tend to be prescribed with original medicines. (9) Since September 2009, Ramathibodi hospital has introduced mandatory generic substation (228 items) for inpatient department. After the policy was implemented, more brand-name drugs were switched to generic with potential cost saving about 10.1 million US$ per year. However, Civil servants and self-pay patients requested the brand-name drug from the outpatient services where the mandatory substitution was not applied. (10)

2.2 Health system in Thailand

2.2.1 Background

At present, there are 3 public health insurance schemes in Thailand: Civil Universal Coverage (UC), Social Security Scheme Servant (SSS) and Medical Benefit Scheme (CSMBS) (37), as shown in table 2.6

Table 2.6 Characteristics of the three public health insurance schemes in Thailand

Characteristics	Public health insurance schemes		
	UC	SSS	CSMBS
Feature	State welfare	Social insurance	Fringe benefit
Legal framework	National Health Security Act B.E.2545(2002)	Social Security Act B.E.2533 (1990)	Medical Benefits for Civil Servants and Public Employees Act B.E.2521 (1978)
Eligible population coverage	Anyone who is not covered by the SSSand CSMBS	All private employees and temporary public employees	All civil servants and permanent public employees, retirees, and their dependent
Population coverage in 2007	46,512,000	7,732,000	4,956,000
Source of finances	General tax revenue	Equal contribution from employers employees, and the Government	General tax revenue
Payment mechanism for health services	Capitation based on hospital expenditure (Capitation contract model)	Capitation based on hospital expenditure (Capitation contract model)	Fee-for-service retrospective reimbursement model
Expenditure per capita (2007Thai Baht)	2,089	2,200	8,462
Ambulatory Services	Public only	Public & Private	Public & Private
Inpatient Services	Public & Private (emergency only)	Public & Private	Public & Private

Table 2.6 Characteristics of the three public health insurance schemes in Thailand (cont.)

Characteristics	Public health insurance schemes		
	UC	SSS	CSMBS
Choice of provider	Contracted hospitals or its network with referral line, registration required	Contracted hospitals or its network with referral line, registration required	Free choice
Brand-name drug	no	no	yes

2.3 Generic policy

The rapid growth on health care expenditure is a major problem in many countries including Thailand. Data from Ministry of Public Health indicated that Thai's health care expenditure increased from 25,315 million baths (3.8 % of gross domestic product-GDP) in 1980 to 588,154 million baths (6.4 % of GDP in 2008). (1) It was also found that drug costs represent a significant proportion of the total health expenditures in Thailand (approximately 46.4 per cent in 2008). (1) The increasing awareness of drug expenditure has led to the increasing use of policy-driven substitution branded drugs to generic drugs (2).

A generic medicine is a drug that is composed of the same medicinal ingredients as the original medicine, but may contain different non-medicinal ingredients. Original medicines and generic medicines are products which have same safety, quality, and efficacy standards. (38) "bioequivalence studies" or"comparative bioavailability" which are the process of generic drug manufacturers, are presented that the generic product has the same standard to the original drug. These processes can be used to prove that their products have same standard of safety and efficacy. In these processes, the blood level of the drug is generally measured after taking a single dose of original drug and the new generic drug when given to a small number of healthy human volunteers. The new generic product has to present that it can be delivered the equal quantity of product at the same proportion of the original drug in

healthy subjects. In case of statin, several studies comparing branded statin with their generic have found them to be clinically equivalent. (16-20)

While generic substitution is obviously found in various cases. Some drug classes need particular consideration, such as narrow therapeutic index medicines, that are products with especially release mechanism, bioengineered protein products, many hormonal products, older drugs marketed before 1938 that were not subject to FDA approval and others with limited bioequivalence data.(39)

On the other hand, therapeutic substitution occurs when patients were switched to an alternative drug, typically from the same class but a different molecule. In practice, therapeutic substitution usually involves a switch from one branded drug to a different generic drug in the same class, as a cost saving measure. However, therapeutic substitution was more likely to involve a subsequent disruption to statin therapy than generic substitution. From observational researches on the results of policy-driven statin substitution, increasing in the risk of mortality or major cardiovascular events was associated with switching atorvastatin to simvastatin. (40-41) Switching to simvastat in from other statins shown that 38% of patients experienced arising in LDL cholesterol levels. (42)

Using of generic medicine was broadly encouraged by the World Health Organization (WHO) according to their relatively lowering price compared with innovator products. (3)In addition, generic drug utilization is a mechanism for reducing drug expenditure in many countries such as the United Kingdom, the United States, the Netherlands, Germany, Denmark and Canada. (43)

In developing countries, substantial saving could be achieved by generic substitution. (44) For low and middle income countries, negative perceptions of stakeholders on quality of generic is barriers to apply generic policies in the same as perverse private sector financial incentive to sell product with the highest profit margin. Other barriers include the absences of generic substitution regulation, physician lack knowledge of price information which is provided by health care provider organizations. (45)

Generic drug utilization policy has been promoted by government for decrease health expenditures in Thailand. Ministry of public health support physician to prescribe generic medicine. Physicians in Thailand are encouraged to write

prescription in generic name or non-proprietary title. In Thailand, many medical schools encourage physician to prescribe generic drug. Many hospitals in Thailand and others countries also support generic substitution policy, which allow pharmacist to substitute generic medicine to patients. In Ramathibodi hospital, which is medical school hospital, generic substitution policy is developed. Pharmacist is allowed to substitute medicine to generic drug except if physician write original name and underlined the original name.

2.4 Factors influencing physicians to prescribe generic drugs

2.4.1 Perception of efficacy and safety of generic

Opinions on generic's efficacy and effectiveness are important factors influencing physician's prescribing decision. (28, 46-49)Most of doctors had a good perception of the government role in assuring the safety and efficacy of generic products (80%) and in encouraging physicians to prescribe generic product (85%). (46)Many General physicians (88.9%) perceived that generic drugs have the same effectiveness as original drugs. (49) Nevertheless, some studies indicated that physicians expressed concerns about all quality and efficacy of generic medication. (48)Several studies found that physicians were neutral to slightly supporting in using of generic medicines. (49-50)

2.4.2 Cost difference

Cost difference is defined as cost difference between original brand and generic drugs. Previous studies showed that cost of medicine is important in physician prescribing. (28, 51-52)

It was found that a large proportion of the general practitioners (76.2%) expressed their need to prescribe low cost medicine (53) and was voluntary to trade off degree of effectiveness to make drugs more affordable for their patients. (52)

Physician may adopt generic prescribing in an effort to improve cost-effectiveness. However, in some cases, original brand may be just as cheap as generic drug. (54)

Although knowledge of drug costs can predict physicians support for cost effective prescribing policies, physician knowledge of drug costs is inadequate. (52, 55-57)

2.4.3 Health insurance scheme

Essential factors to influence physician's decision are drug price, patient's income and patient's insurance coverage. (27-28, 58-61)

Previous studies found that elderly on Medicare are either equally or more tend to be prescribed a original drug. (62-63)

It was also found that self-paying patients were concerned by 94% of physicians in the price of medicines. 68%of physicians were concern when patients had Medicare, and 30% when patients had Medicaid or were participants in a health maintenance organization with a prescription plan. (52)

In Thailand, only generic drugs can be reimbursed for patients under universal coverage scheme (UCS) and social security scheme (SSS). On the other hand, both brand-name drug and generic drug can be reimbursed by patients under civil servant medical benefit scheme (CSMBS).Health insurance scheme was also affected in switching original drug to generic drug too. In Ramathibodi hospital, it was found that statins' expenditure increasing mainly from outpatients of civil servant that are more tend to be prescribed with brand drugs. (9)

2.4.4Characteristics of physician

According to the previous study, the behavior of prescribing most of generic medicines was more general among family physicians who were residency trained, who relied least on drug company representatives, and who were common readers of the New England Journal of Medicine. (64)

A results from systematic review indicated that Physician's prescription decision is affected by their pharmaceutical industry interactions. (65)

It was also found that physicians over the age of 55 years were 3.3 times more tend to report negative attitudes about generic quality, 5.8 times more tend to present that they would not use generics themselves. (48)

2.4.5 Patients preferences

More than half of General Physicians presented needs from patients for special medicines and the major General Physicians generally met their patients' demands or requests from hospital consultants for original drugs. (49, 54, 66)

Negative attitude of generic drugs were associated with lower income, education and non-white race.(67)

Study from AARP Knowledge Management, the study report that insurance companies, requirement from patients and health care plans were affect to prescribe generic drugs from physicians. (47)

2.5 Discrete choice experiments

Discrete choice experiment is an attribute-based survey method for measuring benefits (utility). Discrete choice experiments present respondents with hypothetical scenarios (choice sets) drawn from all possible scenarios (choice sets) accordance with statistical design principles. The choice sets were composed of two or more alternatives, which depend on attributes or characteristics of interest, and respondents have to choose one alternative.(68)

In a Discrete choice experiment participants are proposed a series of choice sets. The individuals are requested to select in one choice set between two or more alternatives. See Table 2.7 for instance of choice set concerning alternative modes of transport to work.

Table 2.7 Example of a discrete choice experiment choice set concerning alternative modes of transport to work. (69)

Attributes	**Car**	**Train**
Duration of transport	20 min	25 min
Walk to/from transportation	0 min	3 min
Price	€ 10	€ 4
My choice	□	□

Attribute Alternative Attribute level

2.5.1 Identifying attribute and level of attribute

Characteristics of scenarios in discrete choice experiments design are called attributes. It is generally perceived that the total amount of attributes in a choice set should not more than six. (70) The attributes of scenarios may include factor such as price, efficacy, dosage, formulation and side effects. The identification and refinement of attribute and attribute levels is not an easy task. For example, for each attribute, a measurement unit must be selected. In most case, the level of attribute is unambiguous. For example, for quantitative attributes such as cost, time, and distance, units can be easily interpreted. However, when using qualitative attribute of which the level be interpreted differently. The researcher need to minimize any ambiguity in the meaning in describing the attribute and its level. Another decision related to the number of levels to assign to each attribute, which need not be the same for all attributes. The more levels might provide a better understanding of the true relationship between an attribute and respondent's utility but there is a trade-off between number of attribute and complexity of the design.

2.5.2 Development of choice set

Discrete choice experiment has 2 methods to design which scenarios will be used in the questionnaire. The first is full factorial design. In the first method, all the possible scenarios are used. This can only be done in designs with limited number of attributes and attribute levels. However, many designs create many possible scenarios which make researcher to select a number of them to take part in the

research. This method is called a fractional factorial design. Fractional factorial design can be done by manually or with computer software. (71)

There are a few of experimental-design approaches that are accessible to the users. The following approaches are summarized. (72)

1. Orthogonal designs that can be construct with manual catalog-based designs. Fold-over, Catalogue and do it by yourself approach involve in manually constructed discrete choice experimental design. Orthogonal main-effects plan (OMEP) is the first think in construct choice question. Profile alternative in each choice question are constructed by this strategies including fold-over, rotated or shifted-design techniques. Some researcher use simply randomly combined pairs from OMEP. The fold-over approach replaces each attribute with its opposite. Rotation each attribute level one place to the right or by wrapping around to the start of the sequence are rotated designs method to create profiles of alternatives in each choice question. Shifted designs use a generator and modular arithmetic (mod Lk) to create alternatives in each choice question.

2. SAS experimental-design macros (SAS macros); Most researchers generally rely on processed that use a computerized algorithm. The SAS system offers a many of experimental-design macros that apply this approach. random selection is a starter of the algorithm. The candidate set of profiles can be an array, an OMEP, or a nearly orthogonal design which incorporates user-specified constraints.

3. Sawtooth software choice-based conjoint designs (Sawtooth software); several form of conjoint analysis can be supported by Sawtooth software more than discrete choice analysis.

The technique of Discrete choice experiment is an attribute-based survey method of benefit, relied on the assumptions that, first, alternatives can be expressed by their characteristics, known as attributes, and second, an participants's appraisal (i.e., benefit, utility, satisfaction or preference) relies on the levels of these attributes (see Table 7). Responses of a Discrete choice experiment are expressed within a benefit (or utility or satisfaction) function which furnishes information on whether or not the given attributes are important; the relative importance of attributes; the rate at which individuals are willing to trade between attributes; and overall benefit scores for alternatives. (73)

The technique of DCE was implemented in health care in the early 1990s. (73) It provides occasions for assessment whether a given health, non-health or service or process attribute of a health care intervention are essential; the relative importance of these various attributes; and the trade-offs individuals are made between these attributes. In addition to other state of preferences techniques such as willingness to pay methods the visual analogue scale to rank, rate or scale alternatives, conjoint analysis methods and time trade-off and standard gamble methods to assess the risk-benefit trade-off of alternatives), a Discrete choice experiment shows a rationally straightforward task and one which more closely resembles a real situation decision (i.e., trading off health outcomes, process attributes and/or non-health outcomes). (74)

The discrete choices observed in a discrete choice experiment are assumed to expose an underlying (latent) utility or benefit function. A participant acting reasonably is anticipated to assess the available alternatives in each choice set and to select the alternative which gives the best utility or benefit, by making trade-offs across the different health outcomes, non-health outcomes and/or process attributes. Thus, a participant will select alternative A over B, if $U(X_A, Z) > U(X_B, Z)$, where U presents the individual's indirect utility function from certain alternatives, X_A present the attributes of alternative A, X_B present the attributes of alternative B, and Z present socioeconomic characteristics of the individual that influence his/her utility. (69) (See in Table 2.8)

Table 2.8 Example of a discrete choice experiment choice set in health care regarding preferences for the provision of benign prostatic hyperplasia drug treatment. (69)

Characteristics of treatment	**Treatment A**	**Treatment B**	**No treatment**
Time to improvement in symptoms	3 months	1 month	No improvement
Treatment reduces the size of prostate	No	Yes	No
Sexual side effects from treatment	Decreased sexual desire	None	None
Non-sexual side effects from treatment	Headache	Dizziness	None
Cost of treatment per month	£30	£50	£0
Chance of having Acute Urinary Retention after 2 years	2%	2%	4%
Chance of requiring surgery after 2 years	4%	6%	4%
Which drug treatment would you prefer?	□	□	□

Random utility theory are use to analyze choices observed in discrete choice experiments (i.e. an error term is included in the utility function to reflect the unobservable factors in the individual's utility function). Hence, a participant will select alternative A over B, if $V(X_A, Z) + \varepsilon_A > V(X_B, Z) + \varepsilon_{B,}$ where V is the measurable component of utility evaluated empirically, and ε_A and ε_B reflect the unobservable factors in the A and B respectively ($X_{A,}$ X_B and Z defined as above). (69)

CHAPTER III
METHOD

This chapter consisted of 5 parts as follows;

3.1 Study design

3.2 Settings

3.3 Participant and sample size

3.4 Study instrument

3.5 Data collection and data analysis

3.1 Study design

This study was a cross sectional survey using discrete choice experiment design. In addition, focus group discussion was also conducted after the survey.

3.2 Settings

Ramathibodi hospital, Bangkok, Thailand

3.3 Participant and sample size

Participants were all family medicine physicians at Ramathibodi hospital. In previous study, family medicine physicians can successfully perform statin generic substitution in routine patients care. (75) In addition, hyperlipidemia can be commonly treated by family medicine physicians.

According to “Using discrete choice experiments to value health and health care”, too large sample size will result in a waste of time, resource and money. On the other hand, too small sample size may lead to inaccurate result. (68) In addition, sample size depends on the budget and resources available. For DCE,

previous study recommended that 20-30 individuals can provide precise parameter estimates. (76)

As the total number of family physicians in Ramathibodi hospital is 46, therefore, all family physicians were invited to participate into the study.

3.4 Study instrument

Self-Administered questionnaire was developed as an instrument in this study. Questionnaires consisted of 4 parts, as follows

3.4.1 General information

This part consisted of questions concerning general information of the respondents such as age, gender, years of experiences in community hospital, years of graduation and frequency of contacting with pharmaceutical representative

3.4.2 Attitude towards generic medicine

This part consisted of 8 questions examining the attitude towards generic medicine. For each question, respondents were asked how strongly, they feel to each statement using a 5-point likert scale, ranging from strongly disagree, disagree, neutral, agree, and strongly agree.

3.4.3 Knowledge about prices of statin

This part consisted of 6 questions examining the knowledge about prices of statin (simvastatin and atorvastatin).

3.4.4 Prescribing decision

This part is a DCE. It consisted of 9 choice set. In choice set, 2 scenarios were given. In each scenario, it was assumed that statin drug was to be prescribed. Participants were then requested to select one scenario that they would prescribe generic statin instead of brand-name statin.

The development of the DCE questions was as follows;

1.) Identification of relevant attributes and attribute levels.

In our study, 4 attributes identified from literature review and expert opinion. The attributes and their levels were described as follows;

1.1 Prevention from Coronary Heart Disease (CHD). This attribute represents the severity of patients. According to the literature review, severity of patients is an important factor associated with generic prescribing decision (31). For statin case, severity of patients can be classified into primary and secondary prevention. According to NCEP guideline, primary prevention can be further classified as Framingham risk score ≥ 2 and 0-1 (31). According to the previous study and expert opinion, switching original statin to generic statin is more feasible to implement and may be cost-saving in primary prevention than in secondary prevention (2).

1.2 Cost difference between statin original drug and statin generic drug per day. This attribute was obtained from literature review that cost difference between original and generic affect whether physician would prescribe original drug or generic drug. Based on the actual cost of brand-name statin and generic statin from database of Ramathibodi hospital, three levels of cost difference were used as follows; 15, 30 and 60 baht per day (36).

1.3 LDL cholesterol level of patient. This attribute also represented severity of patients. Lipid profile of the patients is an important factor associated with decision to prescribe statin according to NCEP guideline. According to expert opinion, LDL cholesterol level has effect on physician's decision whether to prescribe original or generic drug. The LDL-cholesterol level goal depends on patients Framingham risk score (31).According to NCEPIII guideline (31), 3 levels of LDL were specified as follows; 100- 129 mg/dL, 130-159 mg/dL, and > 160 mg/dL, respectively.

1.4 Health insurance scheme. This attribute was derived from literature review and expert opinion that Health insurance scheme has effect on physicians' decision whether or not to prescribe generic. Two levels of attributes are defined as follow; Civil Servant Medical Benefit Scheme (CSMBS) and out of pocket.

The attributes and attribute levels are summarized in table 3.9.

Table 3.9 Attributes and assigned attribute levels

Attribute	**Attribute level**	
Prevention from Coronary Heart Disease (CHD) and framingham risk score	Level 0	Primary prevention (risk score 0-1) (prev1)
	Level 1	Primary prevention (risk score ≥ 2) (prev2)
	Level 2	Secondary prevention (prev3)
Cost difference between statin original drug and statin generic drug per day (simvastatin and atorvastatin)	Level 0	15 baht/day (cost diff1)
	Level 1	30 baht/day (cost diff2)
	Level 2	60 baht/day (cost diff3)
LDL cholesterol level of patient	Level 0	100-129 mg/dL (LDL-C1)
	Level 1	130-159 mg/dL (LDL-C2)
	Level 2	>160 mg/dL (LDL-C3)
Health insurance scheme	Level 0	Civil Servant Medical Benefit Scheme (CSMBS) (Ins1)
	Level 1	Out-of-pocket (Ins2)

2.) Construction of choice set

Fractional factorial design was used to develop scenario in our study. The catalogue of fractional factorial designs has been prepared to facilitate the construction of experimental plans. (72) The catalogue consisted of two part including an index and master plans. The index is a listing and description of the experimental plans contained in the catalogue. The master plan gives the specific combinations of variables for each experimental trial for the plans listed in the index. In our study, three attributes with three levels and one attribute with two levels were specified. According to the index table (shown in Appendix A), the total numbers of experimental trials (choice set) required were nine tests. Index table also indicates the number of master plan and specifies the column used in master plan. As shown in Appendix A, column number 1, 2, 3, 8 of Master plan number 3 were used in this study.

For each attribute, random-pairing method was used to pair attribute level. As shown in appendix B, number of attribute level will be used for pairing method. After random-pairing method was used, the result was shown in table 3.10.

Table 3.10 Construction of choice set

Choice set	Prev		Cost diff		LDL-C		Ins	
	Column 1	Random selection	Column 2	Random selection	column3	Random selection	column 8	Random selection
1	0	1	0	1	0	1	0	0
2	0	2	1	0	1	0	0	1
3	0	0	2	1	2	2	1	1
4	1	0	0	1	1	2	1	0
5	1	2	1	2	2	2	0	1
6	1	1	2	0	0	0	0	0
7	2	1	0	0	2	0	0	0
8	2	0	1	1	0	2	1	0
9	2	0	2	0	1	0	0	0

Prev = Prevention from Coronary Heart Disease (CHD) and framingham risk score: 0 = Primary prevention (risk score 0-1), 1 = Primary prevention (risk score ≥ 2), 2 = Secondary prevention

Cost diff = Cost difference between statin original drug and statin generic drug per day: 0 = 15 baht/day, 1 = 30 baht/day, 2 = 60 baht/day

LDL-C = LDL cholesterol level of patient: 0 = 100-129 mg/dL, 1 = 130-159 mg/dL, 2 = >160 mg/dL

Ins = Health insurance scheme: 0 = Civil Servant Medical Benefit Scheme (CSMBS), 1 = Out-of-pocket

According to table 3.10, example of the first DCE choice set was shown in table 3.11. The developed questionnaire was shown in Appendix C.

Table 3.11 Example of first DCE choice set

Choice set 1		
Attribute	Scenario A	Scenario B
Prevention from Coronary Heart Disease (CHD) and Framingham risk score	Primary prevention (Framingham risk score0-1)	Primary prevention (risk score ≥ 2)
Cost difference between statin original drug and statin generic drug per day (simvastatin and atorvastatin)	15 bath/day	30 bath/day
LDL-C level of patient	100-129 mg/dL	130-159 mg/dL
Health insurance scheme	CSMBS	CSMBS
Given that you are to prescribe statin drug to the patient, what situation do you choose to prescribe generic statin?	Scenario A	~~Scenario B~~

3.5 Data collection and data analysis

3.5.1 Data collection

Pilot testing was conducted among 5 physicians selected by convenient sampling before the actual data collection begins to ensure the clarity and understanding of the questionnaire. The study was approved by the Institutional Review Board at Ramathibodi Hospital before data collection process begins. Questionnaires were distributed to all family physicians along with an information sheet explaining the purpose of the study. Respondents were requested to return the completed questionnaire by dropping it into a return box within 15 days.

After data analysis was completed focus group discussion among 3 physicians was conducted to verify the result of discrete choice experiment as well as to identify possible explanation or other related factors affecting physicians' decision to prescribe generic statin. Three physicians were selected base on willingness to participate and convenience.

3.5.2 Data analysis

Characteristic of sample and attitude toward generic drug were analyzed by using SPSS program version 18

Multinomial logit model was used to analyze factors associated with physician's decision to prescribe generic statin by using STATA program version 11. Example of DCE choice data entry format per one respondent was shown in table 3.12. As shown in table 3.12, 18 rows per respondents were required in our study. In the example, the first choice set of the first respondent is composed of 2 scenarios, as shown in table 3.11. As shown in table 3.12, in the choice set, the respondent selected scenarios B for prescribing generic statin. STATA command for multinomial logit model was shown in Appendix D while STATA command for marginal effect was shown in Appendix E.

Table 3.12 Example of DCE choice data entry format per one respondent

Prev1	Prev2	Prev3	Cost diff1	Cost diff2	Cost diff3	LDL-C1	LDL-C2	LDL-C3	Ins1	Ins2	Sit	Qnno
1	0	0	1	0	0	1	0	0	1	0	0	1
0	1	0	0	1	0	0	1	0	1	0	1	1
1	0	0	0	1	0	0	1	0	1	0	0	2
0	0	1	1	0	0	1	0	0	0	1	1	2
1	0	0	0	0	1	0	0	1	0	1	1	3
1	0	0	0	1	0	0	0	1	0	1	0	3
0	1	0	1	0	0	0	1	0	0	1	1	4
1	0	0	0	1	0	0	0	1	1	0	0	4
0	1	0	0	1	0	0	0	1	1	0	0	5
0	0	1	0	0	1	0	0	1	0	1	1	5
0	1	0	0	0	1	1	0	0	1	0	1	6
0	1	0	1	0	0	1	0	0	1	0	0	6
0	0	1	1	0	0	0	0	1	1	0	0	7
0	1	0	1	0	0	1	0	0	1	0	1	7
0	0	1	0	1	0	1	0	0	0	1	0	8
1	0	0	0	1	0	0	0	1	1	0	1	8
0	0	1	0	0	1	0	1	0	1	0	0	9
1	0	0	1	0	0	1	0	0	1	0	1	9

0 = no, 1 = yes

Prev1 = Primary prevention (risk score 0-1), Prev2 = Primary prevention (risk score $\geq$ 2), Prev3 = Secondary prevention

LDL-C1 = 100-129 mg/dL, LDL-C2 = 130-159 mg/dL, LDL-C3 = >160 mg/dL

Cost diff1 = 15 baht/day, Cost diff2 = 30 baht/day, Cost diff3 = 60 baht/day

Ins1 = Civil Servant Medical Benefit Scheme (CSMBS), Ins2 = Out-of-pocket

Sit = Situation , Qnno = Choice set

CHAPTER IV
RESULT

4.1 Sample Characteristics

Of 46 questionnaires (26 faculty members and 20 residents) sent, 26 completed questionnaires were received, resulting in response rate of 56.52%.Table 4.13 shows the characteristics of the respondents. It was found that 61.5% of the respondents were female. The mean age of respondents was 30.69 years (SD =3.79 years).Average time working in the community hospital was 1.69 years (SD=1.67 years). About 46.2% of the respondents have working experience less than 5 years. Fifteen (57.7%) of respondents meet medical representative 1 time per week.

Table 4.13 Characteristics of the respondents

	N (%) or Mean (SD)
Age (years)	30.69 (3.79)
Sex	
Male	10 (38.5%)
Female	16 (61.5%)
Position	
Faculty member	12 (46.2%)
Resident	14 (53.8%)
Community hospital experience (years)	1.69 (1.67)
Working experience	
< 5 years	12 (46.2%)
5-10 years	8 (30.8%)
>10 years	6 (23.1%)
Frequency of interaction with medical representative	
1 time/wk	15 (57.7%)
2-3 times/wk	8 (30.8%)
4-5 times/wk	3 (11.5%)

4.2 Attitude towards generic drug

Table 4.14 represents attitude towards generic drug of family medicine physicians in the study. Slightly more than half of the respondents agreed that generic drugs are of the same effectiveness as brand- name drugs (n=15; 57.6%)Most of the respondents agreed that generic drugs are as safe as brand name medicines (n=19; 73.1%). Most respondents disagreed that using generic medicines may cause treatment failure (n=22; 84.6%). Regarding the use of generic drug in some therapeutic categories such as narrow therapeutic drugs, about half of the respondents indicated that they hesitate to prescribe generic drugs. Most of the respondents agreed that using generic drug can reduce government health expenditure (n=24; 92.3%).Most respondents indicated that they always prescribe generic medicines to patients (n=25; 96.1%). Only 7.7% of the respondents perceived that patients would be upset if they prescribe generic drugs. Similarly, many respondents were confident to use generic drugs for themselves (n=23; 88.5%).

Table 4.14 Attitude towards generic drug

Statements	Strongly disagree N(%)	Disagree N(%)	Neutral N(%)	Agree N(%)	Strongly agree N(%)
I believe that generic drugs are as effective as brand name drugs.	-	3(11.5)	8(30.8)	14(53.8)	1(3.8)
I believe that generic drugs are as safe as brand name drugs.	-	1(3.8)	6(23.1)	17(65.4)	2(7.7)
I believe that using generic drugs may cause treatment failure.	7(26.9)	15(57.7)	3(11.5)	1(3.8)	-
I hesitate to prescribe generic drug in some class such as narrow therapeutic drugs.	3(11.5)	9(34.6)	9(34.6)	5(19.2)	-
I always prescribe generic drugs to my patients	-	-	1(3.8)	7(26.9)	18(69.2)
Using generic drug can reduce government health expenditure.	-	-	2(7.7)	4(15.4)	20(76.9)
I think when I prescribe generic drug, my patients will be upset.	4(15.4)	12(46.2)	8(30.8)	2(7.7)	-
I feel confident to use generic drugs for myself.	-	-	3(11.5)	15(57.7)	8(30.8)

4.3Knowledge regarding price of statin

Table 4.15 presents knowledge of statin price of physicians, about 57.7% of physicians did not know the price of the simvastatin and atorvastatinin Ramathibodi hospital while 34.6% to 42.3% of physician correctly identified the price of statin drugs.

Table 4.15Knowledge regarding price of statin

Knowledge of Simvastatin price (n=26)		**Zocor® N(%)**	**Bestatin® N(%)**
	Do not know	15(57.7)	15(57.7)
	Know	11(42.3)	11(42.3)
	Not correct	1(3.8)	0 (0)
	Correct	10(38.5)	11(42.3)
Knowledge of Atorvastatin price (n=26)		**Lipitor® N(%)**	**Xarator® N(%)**
	Do not know	15(57.7)	15(57.7)
	Know	11(42.3)	11(42.3)
	Not correct	0 (0)	2(7.7)
	Correct	11(42.3)	9(34.6)

4.4 DCE results

In order to estimate physician's relative preferences in each attribute, the Discrete Choice Experiment data were analyzed by using the Multinomial logit model.The multinomial logit model was specified below;

$$Uisj = \beta1(prevention) + \beta2(costdifference) + \beta3(LDL\text{-}c) + \beta4(insurance) + \varepsilon isj$$

Where the subscript i is an index for the individual, the subscript j is an index for the alternative,the subscript s is number of choice set, the subscript U is utility, the subscript β is coefficients of the observed variables and the subscript ε is error term.

Prevention = Prevention from Coronary Heart Disease (CHD) and Framingham risk score

Cost difference = Cost difference between statin original drug and generic drug per day(simvastatin and atorvastatin)

LDL-c = LDL cholesterol level of patient

Insurance = Health insurance scheme

From the Multinomial logit model, the attributes that were significant determinants of preference of generic statin prescribing were cost difference and health insurance. As shown in table 4.13, physicians preferred to prescribe generic statin if there was very high cost difference between generic and brand-name drug, as compared to low or high cost difference. With respect to health insurance, physicians preferred to prescribe generic statin to self-pay patients more than CSMBS patients.

Result from STATA program for multinomial logit model was shown in Appendix F and Result from STATA program for marginal effect was shown in Appendix G.

Table 4.16 Results of the DCE

Attributes		Coefficient	Standard error	p-value	Marginal effect
Prevention from Coronary Heart Disease (CHD) and Framingham risk score					
	Primary prevention (risk score 0-1)	Reference			
	Primary prevention (risk score ≥ 2)	0.4079	0.5320	0.443	0.0867
	Secondary prevention	-0.3869	0.6325	0.541	-0.0837
Cost difference between statin original drug and statin generic drug per day					
	Cost difference (15 baht/day)	Reference			
	Cost difference (30 baht/day)	0.4179	0.4948	0.398	0.0936
	Cost difference (60 baht/day)	1.1151	0.4343	0.010	0.2480
LDL-C level of patient					
	LDL-c (100-129 mg/dL)	Reference			
	LDL-c (130-159 mg/dL)	0.6093	0.4348	0.161	0.1356
	LDL-c (>160 mg/dL)	0.5007	0.6595	0.448	0.1110
Health Insurance Scheme					
	CSMBS	Reference			
	Out-of-Pocket	2.3791	0.9324	0.011	0.4622

Marginal effect is used to estimate how much the event probability changes when a given predictor is changed by one unit. In term of cost difference, probability of generic prescribing will increase 0.2480 when cost difference was increase from 15 baht/day to 60 baht/day. In addition, probability of generic prescribing will increase 0.4622 if patients were self-pay as comparedto CSMBS.

The focus group was conducted among 3 family physicians (2 were male and 1 was female) after the data analysis. The following questions were asked during focus group.

“Based on the DCE result, physicians preferred to prescribe generic statin if there is very high cost difference between generic and brand name drug, as compared to low or high cost difference. With respect to health insurance physicians, preferred to prescribe generic statin to self-pay patients more than CSMBS patients. On the other hand, prevention of cardiovascular event and LDL-C level are not significant predictors of generic statin prescribing. What is your opinion about the result of the research?”

One of physician who is resident said “I do not concern about health insurance for prescribing generic statin but most of faculty members may consider this factor. Most of them concern about health insurance when they have to make decision whether to prescribe generic or original drug.”

Two physicians mentioned that “For cost difference between original and generic statin, I will ask patients whether they can pay for original or not. If they can pay for original, I will prescribe original to patients.”

When asking about other factors affecting their decision to prescribe statin, one physician said “If patient is received statin at the first time, I will prescribe generic drug. However, if patient is used to receive original statin, I will prescribe original statin as their previous doctor done”.

The other physicians mentioned that “It is difficult to prescribe original drug as policy of Ramathibodi support and promote physicians to prescribe generic drug more than original drug.”

The last physicians told that “I will ask patients whether you are convenience to pay for original statin or not? If they said no, I will change to generic drug.”

When asking about opinion regarding previous 4 factors (Prevention from Coronary Heart Disease (CHD) and Framingham risk score, Cost difference between statin original drug and statin generic drug per day, LDL-C level of patient and Health Insurance Scheme), what is the most important factor affecting to prescribe generic statin to patients and why? And what factor is not important when making decision to prescribe generic statin to patients?

Two of physicians answer that “Prevention from Coronary Heart Disease (CHD) and Framingham risk score is the most important factor that affecting their decision”. The other physician answer that “I consider both Prevention from Coronary Heart Disease (CHD) and Framingham risk score and LDL-C level of patient when decided to prescribe generic statin”

Every physician told that “Health insurance scheme does not affect to physician decision for prescribe generic statin.”

Regarding the DCE questionnaire, 3 respondents mentioned that in some scenario (LDL-C level = 100-129 mg/dL) they might not prescribe statin to patients. On the other hand, they may prefer to adjust behaviors of patient such as increase exercise and control diet

CHAPTER V
DISCUSSION

Similar to the previous studies (28, 46-50), we found that family physicians at Ramathibodi hospital had positive towards generic drug and were more likely to prescribe generic drug to their patients. This result is consistent with previous studies that physicians believe in efficacy and safety of generic drugs. (28, 46-48)The reason of this result may also come from the procurement process of the hospital in which bioequivalence study is required for generic drug. Therefore, physicians in our hospital can believe in efficacy and safety of generic drug. In addition, previous studies in Thailand al so indicated the bioequivalent of generic statin drugs. (18, 21)

With regards to the preferences for generic statin prescribing, LDL cholesterol and prevention from Coronary Heart Disease (CHD) and Framingham risk score were not associated with decision to prescribe generic statin. This may be due to the fact that most physicians in our study had positive towards generic drug and perceived that generic drug were as effective as brand-name drug.

On the other hand, cost difference and health insurance were associated with decision to prescribe generic statin. We found that physicians tend to prescribe generic statin in self-pay patients as compared to CSMBS patients. This findings was consistent with the previous study conducted in Ramathibodi hospital, which found that statins' expenditure increased mainly from civil servant outpatients who were more likely to be prescribed with brand-drugs. (9) Previous study also found that most physician gave stronger consideration to the cost of medications when patients were self-paying, as compared to patients having other kinds of health insurance. (52) This probably due to the fact that the high cost of brand-name drug is not perceived as burden for CSMBS patients as hospital can get reimbursed from The Comptroller General's Department (CGD) directly. In addition, the reimbursement system of CSMBS is fee-for-service so it may create incentive to over-prescribe brand-name drug. Our finding is similar to the previous study which found that financial incentive

to sell products with the highest profit margin was an important barrier for generic substitution policy. (44) On the other hand, in self-pay patients, physician has to consider whether patient can afford to pay for brand-name drug. The result from our focus group discussion also indicated that physicians will ask self-pay patients if they can afford to pay for brand-name drug. However, policy maker should raise awareness in hospital even fee for service is employed; high expenditure of CSMBS is a burden. Expenditure per capita of CSMBS (8,462 baht per capita) is higher thanexpenditure per capita of UC (2,089 baht per capita) and SSS (2,200 baht per capita). (As shown in Table 2.6) Policy-driven of generic substitution should be promoted for reducing health expenditure. In addition, bioequivalence study should be provided for confirmation efficacy of generic drug.

When looking at the price difference, as expected, our study indicated that physicians tended to prescribe generic drug when there was a very high cost difference between original statin and generic statin than low or high cost difference. However, similar to previous studies (45), we also found that many physicians did not know the price of statin. As lack of price information was one barrier for generic substitution (45) and that price difference was important factor determining physician's decision to prescribe generic drug, more effort should be made to educate physicians regarding the price of brand name and generic drug in the hospital. Specially, policy maker may provide information of price of drugs to physicians according to their specialty by giving the price of frequently prescribed drugs for each type of specialist.

Result from focus group is controversial with result from DCE because result from DCE indicated that insurance scheme is an important factors affecting decision to prescribe generic while prevention of CHD and LDL-C level are not important. On the other hand, results from focus group, which were conducted among residence, found that prevention of CHD and LDL-C level are important factors affecting their decision. Nevertheless, physicians from focus group still agree with the result from DCE because they said faculty members might focus on health insurance scheme of the patients when making decision whether to prescribe original or generic statin. Based on the focus group discussion, if the patient was prescribed with brand-name statin at the first time, physicians were less likely to change. Nevertheless, this study does not focus on generic substitution in this case. Further study focusing on

what factors affecting generic substitution is also needed. Reason of different result between focus group and DCE can be explained as follow; Firstly, sample in focus group may not well represent the family medicine physicians as only residents were participated. Only 3 residents were participated in focus group because physicians have limited time. Secondly, asking physician directly in focus group is different from asking by DCE questionnaire because asking indirectly by DCE simulate real complex situation in which respondents gad to make their decision. Thirdly, respondents in focus group were asked in group, which may cause different result. Asking in group may cause social desirability so this is why physicians said they concern in clinical outcome more than cost difference and health insurance scheme. In dept interview should be conducted because it is more convenient to participate and it can avoid influencing answers from other physicians.

Some limitations of our study are needed to be addressed. Firstly, the samples in our study only reflect statin group and family physicians from Ramathibodi hospital. Generalizability to other types of physicians or other settings or other drug groups should be made with caution. It should be noted that different drug groups may have different result. For examples, in the case of antibiotic medicines which are drugs use in acute disease, physician may not concern about cost difference but the effectiveness of drug. This is due to the fact that the ultimate goal of the treatment is to cure the patients within the short period of time. Secondly, it should be noted that our sample size were relatively small (N = 26) although about 56.52% response rate was achieved. According to the previous recommendation (76), the sample size for DCE should be at least 20-30 individuals. Nevertheless, our study provides preliminary yet important results for conducting larger studies on preferences of physicians for generic prescribing. Thirdly, there might be the interaction between attributes, which deserved further studies.

CHAPTER VI
CONCLUSION

We found that family physicians at Ramathibodi hospital had positive towards generic drug and were more likely to prescribe generic drug to their patients. They believe in efficacy and safety of generic drug the same as original drug and believe that using generic drug can reduce government health expenditure. On the other hand, many physicians did not aware of the cost of statin drugs in the hospital.

From DCE result, it was found that physicians tend to prescribe generic statin if there was a very high cost difference between brand-name drug and generic drug. In addition, physicians were more like to prescribe generic statin forself-pay patients more than CSMBS patients.

As the results, policy to support generic prescribing for CSMBS should be formulated. Information on cost of statin drug as well as cost difference between generic drug and brand-name drug should be provided.

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APPENDICES

APPENDIX A

Index table for construct Discrete Choice Experiment

Total No. of Variables	No. of Variable at 2 levels	No. of Variable at 3 levels	No. of Tests Required	Master plan No.	Using Columns No.
4	1	3	9	3	1, 2, 3, 8

APPENDIX B

Master plan 3: 9 trials

Trial	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1	0	0	0	0	0	0	0	0
2	0	1	1	2	0	1	1	0
3	0	2	2	1	0	0	0	1
4	1	0	1	1	1	0	1	1
5	1	1	2	0	1	1	0	0
6	1	2	0	2	1	0	0	0
7	2	0	2	2	0	0	0	0
8	2	1	0	1	0	1	0	1
9	2	2	1	0	0	0	1	0

APPENDIX C

Data Collection Form

<u>คำชี้แจงโครงการวิจัยเรื่อง</u>

<u>การศึกษาปัจจัยในการเลือกสั่งจ่ายยาระหว่างยาต้นแบบ (original) และยาสามัญ (Generic): กรณีการศึกษายาลดไขมันในกลุ่ม HMG-CoA reductase inhibitors (Statins)</u>

เรียน แพทย์แผนกเวชศาสตร์ครอบครัว โรงพยาบาลรามาธิบดี

ปัจจุบันประเทศต่างๆทั่วโลกกำลังเผชิญปัญหาค่าใช้จ่ายทางการแพทย์ที่สูงขึ้นอย่างรวดเร็ว โดยเฉพาะค่าใช้จ่ายด้านยาส่งผลให้มีการสนับสนุนการใช้ยาสามัญ (Generic) มากขึ้น ทั้งนี้ยาลดไขมันในกลุ่ม HMG-CoA reductase inhibitors (Statins) เป็นหนึ่งในกลุ่มยาที่มีมูลค่าการใช้จ่ายสูงและมีการใช้เป็นปริมาณมากในโรงพยาบาลรามาธิบดี การศึกษาครั้งนี้มีวัตถุประสงค์นั้นเพื่อศึกษา ทัศนคติของแพทย์เกี่ยวกับยาสามัญ รวมถึงปัจจัยในการสั่งใช้ยา statin ในรูปแบบยาสามัญของแพทย์แผนกเวชศาสตร์ครอบครัว ที่โรงพยาบาลรามาธิบดี ทั้งนี้ผลการศึกษาที่ได้สามารถนำไปใช้เป็นประโยชน์ในการพัฒนาแนวทางเพื่อส่งเสริมการใช้ยาสามัญในโรงพยาบาลต่อไป

แบบสอบถามนี้ประกอบด้วย 4 ส่วน คือ ข้อมูลทั่วไปของผู้ตอบแบบสอบถาม ทัศนคติต่อการใช้ยาสามัญ ความรู้เกี่ยวกับราคายาต้นแบบ และยาสามัญ ของยากลุ่ม statin และ การเลือกใช้ยาสามัญ statin ในสถานการณ์ต่างๆ

การตอบแบบสอบถามจะใช้เวลาประมาณ 15-20นาที กรุณาตอบคำถามตามความคิดเห็นของท่านอย่างแท้จริง ข้อมูลของท่านจะถูกเก็บเป็นความลับ ผู้วิจัยจะวิเคราะห์และสรุปผลภาพรวมโดยไม่มีการระบุชื่อหรืออ้างอิงถึงตัวบุคคลแต่ประการใด

การวิจัยนี้ไม่อาจเสร็จสมบูรณ์ได้หากไม่ได้รับความอนุเคราะห์จากท่าน คณะผู้วิจัยขอขอบคุณท่านในการให้ข้อมูลไว้ ณ ที่นี้ ด้วย

ภญ.พิภัทรา รอดวรรณะ
ผศ.ดร.ภญ.มนทรัตม์ถาวรเจริญทรัพย์
ดร.พญ.ธัญญรัตน์ อโนทัยสินทวี
ดร.ภญ.ศิตาพร ยังคง

ส่วนที่ 1: ข้อมูลทั่วไปของผู้ตอบแบบสอบถาม

คำชี้แจง กรุณาเติมคำตอบในช่องว่างและทำเครื่องหมาย / ในช่อง ☐ ที่ท่านต้องการเลือก

1. อายุ .....ปี
2. เพศ ☐ ชาย ☐ หญิง
3. ตำแหน่งงานในปัจจุบัน
   ☐ อาจารย์ ☐ แพทย์ประจำบ้าน ☐ แพทย์จ้าง
4. ประสบการณ์การทำงานในโรงพยาบาลชุมชน
   ☐ ไม่มี ☐ มี ระบุ.....ปี
5. ระยะเวลาทำงานหลังจบแพทยศาสตรบัณฑิต
   ☐ น้อยกว่า 5 ปี ☐ 5-10 ปี ☐ มากกว่า 10 ปี
6. จำนวนครั้งที่พบผู้แทนยาต่อสัปดาห์
   ☐ 1 ครั้ง ต่อ สัปดาห์ ☐ 2-3 ครั้ง ต่อ สัปดาห์ ☐ 4-5 ครั้ง ต่อ สัปดาห์

กรุณาทำแบบสอบถามในส่วนที่ 2 ในหน้าถัดไป

ส่วนที่ 2: ทัศนคติต่อการใช้ยาสามัญ (Generic)

คำชี้แจง กรุณาทำเครื่องหมาย / ในช่อง ☐ ที่ท่านต้องการเลือก

ทัศนคติต่อการใช้ยาสามัญ	ไม่เห็นด้วยมากที่สุด	ไม่เห็นด้วย	เฉยๆ	เห็นด้วย	เห็นด้วยมากที่สุด
7.ยาสามัญ (Generic drug) มีประสิทธิภาพเทียบเท่ากับยาต้นแบบ (Original drug)					
8.ยาสามัญ (Generic drug) มีความปลอดภัยเทียบเท่ากับยาต้นแบบ (Original drug)					
9.การใช้ยาสามัญ (Generic drug)จะก่อให้เกิดการล้มเหลวของการรักษา					
10.ฉันลังเลที่จะจ่ายยาสามัญ (Generic drug) ในบางกลุ่มยา เช่น narrow therapeutic drug กับผู้ป่วยของฉัน					
11.ฉันมักจะจ่ายยาด้วยยาสามัญ (Generic drug)ให้กับผู้ป่วย					
12.การใช้ยาสามัญ (Genericdrug) สามารถช่วยประยัดค่าใช้จ่ายให้กับรัฐบาลได้มาก					
13.ฉันคิดว่าผู้ป่วยจะไม่พอใจหากจ่ายยา ยาสามัญ (Generic drug)					
14. ฉันมั่นใจที่จะใช้ยาสามัญเพื่อรักษาอาการเจ็บป่วยของตนเอง					

กรุณาทำแบบสอบถามในส่วนที่ 3 ในหน้าถัดไป

ส่วนที่ 3: ความรู้เกี่ยวกับราคายาต้นแบบ (original drug) และยาสามัญ (Generic) ของยากลุ่ม statin

15. ท่านทราบราคาของ Simvastatin ของโรงพยาบาลรามาธิบดีหรือไม่

☐ ทราบ ☐ ไม่ทราบ (**ข้ามไปทำข้อ** 18)

16. ราคาของ Simvastatin ที่เป็นยาต้นแบบ (original) คือ

☐ < 20 บาท/เม็ด ☐ 21-30 บาท/เม็ด ☐ > 31 บาท/เม็ด

17. ราคาของ simvastatin ที่เป็นยาสามัญ (Generic) คือ

☐ 1-5 บาท/เม็ด ☐ 6-10 บาท/เม็ด ☐ > 11 บาท/เม็ด

18. ท่านทราบราคายาของ Atorvastatinของโรงพยาบาลรามาธิบดีหรือไม่

☐ ทราบ ☐ ไม่ทราบ **(ข้ามไปทำส่วนที่ 4)**

19. ราคาของ Atorvastatin ที่เป็นยาต้นแบบ (original) คือ

☐ < 20 บาท/เม็ด ☐ 21-40 บาท/เม็ด ☐ >41 บาท/เม็ด

20. ราคาของ Atorvastatin ที่เป็นยาสามัญ (Generic)คือ

☐ < 20 บาท/เม็ด ☐ 21-40 บาท/เม็ด ☐ >41 บาท/เม็ด

กรุณาทำแบบสอบถามในส่วนที่ 4 ในหน้าถัดไป

ส่วนที่ 4: การเลือกใช้ยาสามัญstatin ในสถานการณ์ต่างๆ

คำชี้แจง

ในการตอบแบบสอบถามในส่วนนี้ ขอให้ท่านจินตนาการว่าท่านกำลังจะสั่งใช้ยาลดไขมันในเลือดในกลุ่ม HMG-CoA reductase inhibitors (Statins) ให้กับผู้ป่วยที่มีระดับไขมันสูงซึ่งได้ผ่านการประเมินเบื้องต้นแล้วว่ามีความเหมาะสมที่จะใช้ยาในกลุ่มดังกล่าว

แบบสอบถามในส่วนนี้ มีทั้งหมด 9 ข้อ (ชุดตัวเลือก) ในแต่ละข้อจะประกอบด้วยสถานการณ์ A และสถานการณ์ B ซึ่งมีคุณลักษณะแตกต่างกัน โปรดพิจารณาคุณลักษณะของแต่ละสถานการณ์เปรียบเทียบกัน โดยในทั้งสองสถานการณ์ผู้ป่วยจำเป็นต้องได้รับยา statin กรุณาเลือกสถานการณ์ที่ท่านจะเลือกสั่งยา statin **ในรูปแบบยาสามัญ**ให้กับผู้ป่วย (หากจำเป็นต้องเลือก 1 สถานการณ์) โดยทำเครื่องหมาย x ลงในช่อง ☐ ที่ท่านเลือก ดังตัวอย่างข้างล่าง

ตัวอย่าง

ชุดตัวเลือกที่ X		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score0-1)	Secondary prevention
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	15บาทต่อวัน	30บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	130-159 mg/dL	>160 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	~~**สถานการณ์** A~~	**สถานการณ์** B

หมายเหตุ

ยาสามัญ (Generic) หมายถึง ยาที่มีตัวยาที่ใช้รักษาโรคตัวเดียวกับยาต้นแบบ ซึ่งจะให้ผลรักษา ผลข้างเคียง ปริมาณยาที่ใช้ และวิธีการต่างๆในการใช้ยา เช่นเดียวกับยาต้นแบบ แต่มีราคาถูกกว่า หรืออาจเข้าใจกันในคำว่า local made ตัวอย่างของ ยาสามัญในกรณีของ Simvastatin ได้แก่Bestatin, Zimmexเป็นต้น

ยาต้นแบบ (Original) หมายถึง ยารักษาโรคต่างๆที่ผ่านการวิจัย, พัฒนา, ผลิตและคิดค้นได้เป็นยาตัวแรกจากบริษัทผู้ผลิตกรณีของ Simvastatin หมายถึง Zocor® กรณีของ atorvastatinหมายถึง Lipitor ®

ชุดตัวเลือกที่1		
คุณลักษณะ	**สถานการณ์ A**	**สถานการณ์ B**
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score0-1)	Primary prevention (Framingham risk score≥ 2)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	15 บาทต่อวัน	30 บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	100-129 mg/dL	130-159 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์ A**	**สถานการณ์ B**

ชุดตัวเลือกที่ 2		
คุณลักษณะ	**สถานการณ์ A**	**สถานการณ์ B**
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score0-1)	Secondary prevention
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	30บาทต่อวัน	15บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	130-159 mg/dL	100-129 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ชำระเงินเอง
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์ A**	**สถานการณ์ B**

ชุดตัวเลือกที่ 3		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score0-1)	Primary prevention (Framingham risk score0-1)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	60บาทต่อวัน	30 บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	>160 mg/dL	>160 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ชำระเงินเอง	ชำระเงินเอง
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์** A	**สถานการณ์** B

ชุดตัวเลือกที่ 4		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score$\geq$ 2)	Primary prevention (Framingham risk score0-1)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	15 บาทต่อวัน	30 บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	130-159mg/dL	>160 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ชำระเงินเอง	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์** A	**สถานการณ์** B

ชุดตัวเลือกที่ 5		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score≥ 2)	Secondary prevention
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	30บาทต่อวัน	60 บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	>160 mg/dL	>160 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ชำระเงินเอง
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์** A	**สถานการณ์** B

ชุดตัวเลือกที่ 6		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Primary prevention (Framingham risk score≥ 2)	Primary prevention (Framingham risk score≥ 2)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	60บาทต่อวัน	15บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	100-129 mg/dL	100-129 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์** A	**สถานการณ์** B

ชุดตัวเลือกที่ 7		
คุณลักษณะ	**สถานการณ์ A**	**สถานการณ์ B**
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Secondary prevention	Primary prevention (risk score $\geq$ 2)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) และยาสามัญ (Generic drug)ต่อวัน	15 บาทต่อวัน	15บาทต่อวัน
ระดับ LDL-c ของผู้ป่วย	>160 mg/dL	100-129 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์ A**	**สถานการณ์ B**

ชุดตัวเลือกที่ 8		
คุณลักษณะ	**สถานการณ์ A**	**สถานการณ์ B**
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Secondary prevention	Primary prevention (risk score = 0-1)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) และยาสามัญ (Generic drug)ต่อวัน	30บาทต่อวัน	30 บาทต่อวัน
ระดับ LDL-c ของผู้ป่วย	100-129 mg/dL	>160 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ชำระเงินเอง	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์ A**	**สถานการณ์ B**

ชุดตัวเลือกที่ 9		
คุณลักษณะ	**สถานการณ์** A	**สถานการณ์** B
การป้องกันโรคหลอดเลือดหัวใจ (Framingham risk score)	Secondary prevention	Primary prevention (risk score = 0-1)
ราคาที่แตกต่างกันระหว่างยาต้นแบบ (Original drug) **และยาสามัญ** (Generic drug)**ต่อวัน**	60บาทต่อวัน	15บาทต่อวัน
ระดับ LDL-c **ของผู้ป่วย**	130-159mg/dL	100-129 mg/dL
สิทธิการประกันสุขภาพของผู้ป่วย	ข้าราชการ	ข้าราชการ
จากคุณลักษณะดังกล่าวท่านจะเลือกใช้ยาสามัญ (Generic drug)statin **ในสถานการณ์ใด**	**สถานการณ์** A	**สถานการณ์** B

ผู้วิจัยขอขอบพระคุณเป็นอย่างยิ่งที่ท่านกรุณาตอบแบบสอบถามจนเสร็จสมบูรณ์

APPENDIX D

STATA command for multinomial logit model

list if prevention1==0 & prevention2==0 & prevention3==0

list if cost difference1==0 & cost difference2==0 & cost difference3==0

list if ldlc1==0 & ldlc2==0 & ldlc3==0

list if insurance1==0 & insurance2==0

global X "prevention2 prevention3 costdifference2 costdifference3 ldlc2 ldlc3 insurance2"

clogit situation $X, group(qnno)

APPENDIX E

STATA command for marginal effect

```
cap program drop mareff
program define mareff

qui {
replace prevention1 = 1
replace prevention2 = 0
replace prevention3 = 0
predict pprevention1
replace prevention1 = 0
replace prevention2 = 1
predict pprevention2
replace prevention2 = 0
gen mprevention2 = pprevention2 - pprevention1
sum mprevention2
sca me_prevention2 = r(mean)
replace prevention3 = 1
predict pprevention3
gen mprevention3 = pprevention3 - pprevention1
sum mprevention3
sca me_prevention3 = r(mean)
drop pprevention* mprevention*
replace prevention1 = copyprevention1
replace prevention2 = copyprevention2
replace prevention3 = copyprevention3
noi di me_prevention2, me_prevention3
```

```
replace costdifference1 = 1
replace costdifference2 = 0
replace costdifference3 = 0
predict pcostdifference1
replace costdifference1 = 0
replace costdifference2 = 1
predict pcostdifference2
replace costdifference2 = 0
gen mcostdifference2 = pcostdifference2 - pcostdifference1
sum mcostdifference2
sca me_costdifference2 = r(mean)
replace costdifference3 = 1
predict pcostdifference3
gen mcostdifference3 = pcostdifference3 - pcostdifference1
sum mcostdifference3
sca me_costdifference3 = r(mean)
drop pcostdifference* mcostdifference*
replace costdifference1 = copycostdifference1
replace costdifference2 = copycostdifference2
replace costdifference3 = copycostdifference3
noi di me_costdifference2, me_costdifference3

replace ldlc1 = 1
replace ldlc2 = 0
replace ldlc3 = 0
predict pldlc1
replace ldlc1 = 0
replace ldlc2 = 1
predict pldlc2
replace ldlc2 = 0
gen mldlc2 = pldlc2 - pldlc1
sum mldlc2
```

```
sca me_ldlc2 = r(mean)
replace ldlc3 = 1
predict pldlc3
gen mldlc3 = pldlc3 - pldlc1
sum mldlc3
sca me_ldlc3 = r(mean)
drop pldlc* mldlc*
replace ldlc1 = copyldlc1
replace ldlc2 = copyldlc2
replace ldlc3 = copyldlc3
noi di me_ldlc2, me_ldlc3

replace insurance1 = 1
replace insurance2 = 0
predict pinsurance1
replace insurance1 = 0
replace insurance2 = 1
predict pinsurance2
gen minsurance2 = pinsurance2 - pinsurance1
sum minsurance2
sca me_insurance2 = r(mean)
drop pinsurance* minsurance*
replace insurance1 = copyinsurance1
replace insurance2 = copyinsurance2
noi di me_insurance2
}
end
noi xi: logit situation $X i.qnno
noi xi: logistic situation $X i.qnno
noi mareff
```

APPENDIX F

Result from STATA program for multinomial logit model

note: multiple positive outcomes within groups encountered.

Iteration 0: log likelihood = -276.54246
Iteration 1: log likelihood = -274.75564
Iteration 2: log likelihood = -274.75165
Iteration 3: log likelihood = -274.75165

Conditional (fixed-effects) logistic regression Number of obs = 468
LR chi2(7) = 59.57
Prob > chi2 = 0.0000
Log likelihood = -274.75165 Pseudo R2 = 0.0978

Situation	**Coef.**	**Std. Err.**	**Z**	**P>|z**	**[95% Conf. Interval]**
prevention2	.4078646	.532036	0.77	0.443	-.6349067 1.450636
Prevention3	-.3869362	.6325088	-0.61	0.541	-1.626631 .8527582
costdiffer~2	.417891	.4948338	0.84	0.398	-.5519654 1.387747
costdiffer~3	1.115137	.4343078	2.57	0.010	.2639093 1.966365
ldlc2	.6093112	.434772	1.40	0.161	-.2428262 1.461449
ldlc3	.5006548	.6594856	0.76	0.448	-.7919132 1.793223
insurance2	2.379114	.9323908	2.55	0.011	.5516614 4.206566

APPENDIX G

Result from STATA program for marginal effect

Noi marreff
0.0867227 -0.08369941
0.09358992 0.24799926
0.13555688 0.11100923
0.46221459

APPENDIX H

คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
๒๗๐ ถนนพระราม ๖ แขวงทุ่งพญาไท เขตราชเทวี กทม. ๑๐๔๐๐
โทร. (๐๒) ๒๐๑-๑๐๐๐

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Documentary Proof of Ethical Clearance
Committee on Human Rights Related to Research Involving Human Subjects
Faculty of Medicine Ramathibodi Hospital, Mahidol University

MURA2014/335

Title of Project	Factor Influencing Physician's Decision on Generic Drug Prescription: A Case Study of Statin
Protocol Number	ID 06-57-39
Principal Investigator	Miss. Pipattra Rodvanna
Official Address	Faculty of Pharmacy Mahidol University

The aforementioned project has been reviewed and approved by the Committee on Human Rights Related to Research Involving Human Subjects, based on the Declaration of Helsinki.

Signature of Secretary Committee on Human Rights Related to Research Involving Human Subjects	..... Prof. Duangrurdee Wattanasirichaigoon, M.D.
Signature of Chairman Committee on Human Rights Related to Research Involving Human Subjects	..... Prof. Pratak O-Prasertsawat, M.D.
Date of Approval	June 23, 2014
Duration of Study	4 Months

BIOGRAPHY

NAME	Miss. Pipattra Rodvanna
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